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On 23 Jan. 2007

TOWNSEND and TOWNSEND and CREW LLP

By *Malinda Adagis*

PATENT  
Attorney Docket No.: 016285-003710US  
Client Ref. No.: 02/MED/122

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Yuk-Ming Dennis Lo et al.

Application No.: 10/759,783

Filed: January 16, 2004

For: CIRCULATING MRNA AS  
DIAGNOSTIC MARKERS

Customer No.: 20350

Confirmation No. 8146

Examiner: MYERS, Carla J.

Technology Center/Art Unit: 1634

DECLARATION UNDER 37 C.F.R. §1.132  
OF DR. ROSSA CHIU AND DR. DENNIS  
LO

Mail Stop AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

We, Rossa Wai Kwun Chiu and Yuk Ming Dennis Lo, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both (18 U.S.C. § 1001), and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

I. All statements herein made of our own knowledge are true, and statements made on information or belief are believed to be true and correct.

2. I, Rossa Wai Kwun Chiu, received a Bachelor degree in Medicine and Surgery from The University of Queensland, Australia, and a Doctor of Philosophy degree in Chemical Pathology from the Chinese University of Hong Kong, Hong Kong. Currently, I am Professor 2 at The Chinese University of Hong Kong. I have been at this and related positions for 7 years. A copy of my curriculum vitae is attached as Exhibit A.

3. I, Yuk Ming Dennis Lo, received a Bachelor of Arts degree and a Master of Arts degree from the University of Cambridge, United Kingdom, and a Bachelor degree in Medicine and Surgery, a Doctor of Philosophy degree, and a Doctor of Medicine degree from the University of Oxford, United Kingdom. Currently, I am Professor of Chemical Pathology at The Chinese University of Hong Kong. I have been at this and related positions for 10 years. A copy of my curriculum vitae is attached as Exhibit B.

4. The invention of the above-referenced patent application provides, for the first time, a method for diagnosing or predicting preeclampsia in a pregnant woman, based on the detection of an increase in the amount of human corticotropin releasing hormone (hCRH) mRNA in the pregnant woman's serum or plasma.

5. We are named inventors on this patent application. We have read and are familiar with the contents of this application. In addition, we have read the Office Action mailed July 25, 2006, for this application. It is our understanding that the pending claims have been rejected because the Examiner questions whether the claimed method is fully enabled for its intended scope, particularly when used in women who are not in the third trimester of their pregnancy. This declaration is provided to establish that the claimed method is generally effective for diagnosing or predicting preeclampsia in pregnant women. The research described below was performed under our directions and we have personal knowledge of the research.

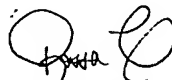
6. To demonstrate the correlation between plasma/serum level of hCRH mRNA and preeclampsia in pregnant women outside of the third trimester, plasma samples were collected from women between 11 and 13 weeks of gestation (*i.e.*, first trimester). The maternal

plasma samples were stored frozen until delivery. During the course of pregnancy, those who eventually developed preeclampsia were noted. Among the women involved in this study, four developed preeclampsia. Maternal plasma samples were retrieved from these four cases together with the samples from those who did not develop preeclampsia or other complications (*i.e.*, normal controls). Each preeclamptic case was matched to six or seven normal controls with comparable gestational ages and sample storage time. Each preeclamptic case together with the matched controls was named as group A, B, C, or D.

7. Plasma hCRH mRNA concentrations were then assessed by real-time quantitative RT-PCR. The hCRH mRNA concentration of each preeclamptic case was compared with the normal control cases within its constituent group. Within each group, the samples were ranked in ascending order in accordance with the increasing maternal plasma hCRH mRNA level. The results are depicted in the attached graph (Exhibit C). The preeclamptic cases are indicated by the crosses, whereas the normal control cases are indicated by the open circles. Among 3 of the 4 groups, the preeclamptic cases show a consistently higher plasma hCRH mRNA concentration in comparison with its relevant controls.

8. In summary, the data of our studies clearly demonstrate that: (1) hCRH mRNA is readily detectable in first trimester maternal plasma; and (2) there is a strong correlation between an increase level of plasma hCRH mRNA and a heightened risk of preeclampsia. Thus, the method as claimed in this patent application is generally effective for diagnosing or predicting preeclampsia in pregnant women, not just limited to those in their third trimester.

Date: 19 JAN 2007

By:   
\_\_\_\_\_  
Rossa Wai Kwun Chiu, MBBS, Ph.D.

Appl. No. 10/759,783  
Declaration of Dr. Wai Kwun Rossa Chiu  
under 37 CFR 1.132

PATENT

Date: 19 Jan 2007

By: 

Yuk Ming Dennis Lo, MA DM DPhil BM BCh

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Attachment (Exhibits A-C)  
CG/cg  
60957918 v1



# Exhibit A

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*CURRICULUM VITAE*

**ROSSA WAI KWUN CHIU**

Present position:     Lecturer (Professor 2)  
                             Department of Chemical Pathology  
                             The Chinese University of Hong Kong

Affiliated College:    United College

Phone:                 2632 2348  
Fax:                    2636 5090  
Email:                 rossachiu@cuhk.edu.hk

Date of birth:         30<sup>th</sup> July 1974  
Place of birth:        United Kingdom  
Marital status:        Married with 2 children

**ACADEMIC AND PROFESSIONAL QUALIFICATIONS:**

2005                    Fellow of the Hong Kong Academy of Medicine  
                             (FHKAM(Pathology))  
                             Hong Kong

2005                    Fellow of the Hong Kong College of Pathologists (FHKCPath)  
                             Hong Kong

2004                    Fellow of the Royal College of Pathologists of Australasia  
                             (FRCPA)  
                             Australia

2004                    Doctor of Philosophy in Chemical Pathology (PhD)  
                             The Chinese University of Hong Kong  
                             Hong Kong

1997                    Bachelor of Medicine and Bachelor of Surgery (MBBS)  
                             First Class Honours  
                             The University of Queensland  
                             Australia

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## **EMPLOYMENT HISTORY:**

Aug 2006 to present    Professor 2  
                                 Department of Chemical Pathology  
                                 The Chinese University of Hong Kong

Sep 2006 to present    Honorary Consultant  
                                 Department of Chemical Pathology  
                                 Prince of Wales Hospital, Hong Kong

Jun 2004 to Jul 2006    Lecturer (Associate Professor)  
                                 Department of Chemical Pathology  
                                 The Chinese University of Hong Kong

Jul 1999 to Jun 2004    Lecturer (Assistant Professor)  
                                 Department of Chemical Pathology  
                                 The Chinese University of Hong Kong

Jul 1999 to Sep 2006    Honorary Medical Officer  
                                 Department of Chemical Pathology  
                                 Prince of Wales Hospital, Hong Kong

Jan 1999 to Jul 1999    Medical Officer  
                                 Department of Chemical Pathology  
                                 Prince of Wales Hospital, Hong Kong

Jan to Dec 1998        House Officer  
                                 Hospital Authority, Hong Kong

## **TEACHING**

### **TEACHING AWARDS:**

2006                    Outstanding Intern's Practice Tips Workshop in 2005/2006

2005                    Master teacher 1999/2000 – 2003/2004, Faculty of Medicine

2005                    "Teacher of the Year: Medical Year Three" for 2003-2004

2004                    "Teacher of the Year: Medical Year Three" for 2002-2003

2003                    "Teacher of the Year: Medical Year Three" for 2001-2002

2002                    "Teacher of the Year: Medical Year Three" for 2000-2001

2001                    "Teacher of the Year: Medical Year Three" for 1999-2000

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## **POSTGRADUATE SUPERVISION**

Supervision of 1 MPhil student.

Co-supervision of 1 PhD and 1 MPhil students.

## **RESEARCH**

### **RESEARCH INTERESTS:**

- Non-invasive prenatal diagnosis
- Clinical applications and biology of circulating nucleic acids
- Development of novel molecular diagnostic approaches
- Impact of preanalytical variables in molecular analyses
- Molecular epidemiological investigation of infectious diseases

Prenatal investigations are an integral and important part of modern obstetrics care. Major advances in molecular genetics have led to the development of services, such as genetic counselling, prenatal and preimplantation diagnosis, that cater for the investigation of fetal genetic and chromosomal abnormalities. In recent years, extra demands have been placed on these services as a result of the emerging sociocultural trend to delay childbirth and to maintain smaller family units. However, current prenatal investigative programmes rely on fetal tissue sampling procedures such as amniocentesis and chorionic villus sampling for the provision of a confirmatory diagnosis. By virtue of their invasive nature, these procedures are associated with a risk of spontaneous abortion. Being intrigued by this clinical dilemma, I have developed interests in the research for safer alternatives to conventional prenatal diagnostic procedures.

The recent discovery of the existence of fetal nucleic acids in plasma and serum of pregnant women has led to new exciting possibilities for the development of non-invasive prenatal diagnostic approaches. However, during the initial years, not much was known about this newly described phenomenon and its diagnostic potential was not fully realised. Hence, my research focuses on exploring the biological characteristics of circulating fetal nucleic acids and furthering the development of new applications on non-invasive prenatal diagnosis or monitoring. As the ultimate aim of this line of research is to bring non-invasive prenatal diagnosis to the realms of clinical practice, my research interest also involves the studying of variables which would affect the reliability of the newly developed prenatal diagnostic tests. Furthermore, in order to develop new strategies for non-invasive prenatal diagnosis, novel molecular approaches would have to be employed, which has since become another area of my research interest.



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## RESEARCH AWARDS:

- 2006      Young Scientist Award  
International Society for Prenatal Diagnosis  
13<sup>th</sup> International Conference on Prenatal Diagnosis and Therapy,  
28-31 May, 2006, Kyoto, Japan
- 2005      Young Researcher Award  
The Chinese University of Hong Kong
- 2003      Silver Medal, Best original research by trainees  
Hong Kong Academy of Medicine
- 2003      Outstanding Young Investigator  
Circulating Nucleic Acids in Plasma and Serum III  
9-11 November 2003, Santa Monica, USA
- 2002      Young Scientist Award in Life Science  
Hong Kong Institution of Science
- 2002      “The Top Four Winner Awards of Poster Presentation”  
4<sup>th</sup> Human Genome Organization Pacific Meeting  
27-30 October 2002, Pattaya, Thailand
- 2002      “Asia B” poster award  
18<sup>th</sup> International Congress of Clinical Chemistry and Laboratory  
Medicine, 20-26 October 2002, Kyoto, Japan

## RESEARCH OUTPUT:

### *Refereed Journal Publications* (in reverse chronological order)

1. **Chiu, RWK**, Chim, SSC, Wong, IHN, Wong, CSC, Lee, WS, To, KF, Tong, JHM, Yuen, RKC, Shum, ASW, Chan, JKC, Chan, LYS, Yuen, JWF, Tong, YK, Weier, JF, Ferlatte, C, Leung, TN, Lau, TK, Lo, KW and Lo, YMD (In press). Hypermethylation of RASSF1A in human and rhesus placentas. *Am J Pathol*.
2. Lo, YMD, Tsui, NBY, **Chiu, RWK**, Lau, TK, Leung, TN, Heung, MMS, Gerovassili, A, Jin, Y, Nicolaides, K, Cantor, CR and Ding, C (2007). Plasma placental RNA allelic ratio permits noninvasive prenatal chromosomal aneuploidy detection. *Nat Med* Jan 7.

3. Lo, YMD and **Chiu, RWK** (2007). Prenatal diagnosis: Progress through plasma nucleic acids. *Nat Rev Genet* 8, 71-77.
4. Chan, KCA, Ding, C, Gerovassili, A, Yeung, SW, **Chiu, RWK**, Leung, TN, Lau, TK, Chim, SSC, Chung, GTY, Nicolaides, KH and Lo, YMD (2006). Hypermethylated RASSF1A in Maternal Plasma: A Universal Fetal DNA Marker that Improves the Reliability of Noninvasive Prenatal Diagnosis. *Clin Chem* 52, 2211-2218.
5. Tong, YK, Ding, C, **Chiu, RWK**, Gerovassili, A, Chim, SSC, Leung, TY, Leung, TN, Lau, TK, Nicolaides, KH and Lo, YMD (2006). Noninvasive Prenatal Detection of Fetal Trisomy 18 by Epigenetic Allelic Ratio Analysis in Maternal Plasma: Theoretical and Empirical Considerations. *Clin Chem* 52, 2194-2202.
6. Pang, RT, Poon, TCW, Chan, KCA, Lee, NL, **Chiu, RWK**, Tong, YK, Chim, SSC, Sung, JJ, Lo, YMD (2006). Serum amyloid A is not useful in the diagnosis of severe acute respiratory syndrome. *Clin Chem* 52, 1202-1204.
7. Rainer, TH, Lam, NYL, Man, CY, **Chiu, RWK**, Woo, KS and Lo, YMD (2006). Plasma beta-globin DNA as a prognostic marker in chest pain patients. *Clin Chim Acta* 368, 110-113.
8. **Chiu, RWK**, Jin, Y, Chung, GTY, Lui, WB, Chan, ATC, Lim, W and Lo, YMD (2006). Automated extraction protocol for quantification of SARS-Coronavirus RNA in serum: an evaluation study. *BMC Infect Dis* 6, 20.
9. **Chiu, RWK**, Lui, WB, Cheung, MC, Kumta, N, Farina, A, Banzola, I, Grotti, S, Rizzo, N, Haines, CJ and Lo, YMD (2006). Time profile of appearance and disappearance of circulating placenta-derived mRNA in maternal plasma. *Clin Chem* 52, 313-316.
10. Pang, RT, Poon, TC, Chan, KCA, Lee, NL, **Chiu, RWK**, Tong, YK, Wong, RM, Chim, SSC, Ngai, SM, Sung, JJ and Lo, YMD (2006). Serum proteomic fingerprints of adult patients with severe acute respiratory syndrome. *Clin Chem* 52, 421-429.
11. **Chiu, RWK**, Rainer, TH and Lo, YMD (2005). Circulating nucleic acid analysis: diagnostic applications for acute pathologies. *Acta Neurochir Suppl* 95, 471-474.
12. Tsui, NBY, **Chiu, RWK**, Ding, C, El-Sheikhah, A, Leung, TN, Lau, TK, Nicolaides, KH and Lo, YMD (2005). Detection of Trisomy 21 by Quantitative Mass Spectrometric Analysis of Single Nucleotide Polymorphisms. *Clin Chem* 51, 2358-2362.

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13. **Chiu, RWK**, Chan, CWM, Zhong, XY, Lapaire, O, Holzgreve, W, Hahn, S and Lo, YMD (2005). Fetal rhesus D mRNA is not detectable in maternal plasma. *Clin Chem* 51, 2210-2211.
  14. **Chiu, RWK**, Lui, WB, El-Sheikhah, A, Chan, ATC, Lau, TK, Nicolaides, KH and Lo, YMD (2005). Comparison of protocols for extracting circulating DNA and RNA from maternal plasma. *Clin Chem* 51, 2209-2210.
  15. Chung, GTY, **Chiu, RWK**, Cheung, JLK, Jin, YJ, Chim, SSC, Chan, PKS and Lo, YMD (2005). A simple and rapid approach for screening of SARS-coronavirus genotypes: an evaluation study. *BMC Infect Dis* 5, 87.
  16. \*Chim, SSC, \*Tong, YK, \***Chiu, RWK**, Lau, TK, Leung, TN, Chan, LYS, Oudejans, CBM, Ding, C and Lo, YMD (2005). Detection of the placental epigenetic signature of the maspin gene in maternal plasma. *Proc Natl Acad Sci U S A* 102, 14753-14758. (Equal first author)
  17. Wong, BCK, **Chiu, RWK**, Tsui, NBY, Chan, KCA, Chan, LW, Lau, TK, Leung, TN and Lo, YMD (2005). Circulating Placental RNA in Maternal Plasma Is Associated with a Preponderance of 5' mRNA Fragments: Implications for Noninvasive Prenatal Diagnosis and Monitoring. *Clin Chem* 51, 1786-1795.
  18. Cheng, FW, Ng, EKO, Li, AM, Hon, EK, **Chiu, RWK**, Lo, YMD and Ng, PC (2005). Clinical, virologic and immunologic profiles of a young infant with severe acute respiratory syndrome. *Pediatr Infect Dis J* 24, 567-568.
  19. Chung, GTY, **Chiu, RWK**, Chan, KCA, Lau, TK, Leung, TN, Chan LW and Lo, YMD (2005). Detrimental Effect of Formaldehyde on Plasma RNA Detection. *Clin Chem* 51, 1074-1076.
  20. Chan, KCA, Tang, NLS, Hui, DSC, Chung, GTY, Wu, AK, Chim, SSC, **Chiu, RWK**, Lee, N, Choi, KW, Sung, YM, Chan, PK, Tong, YK, Lai, ST, Yu, WC, Tsang, O and Lo, YMD (2005). Absence of association between angiotensin converting enzyme polymorphisms and development of adult respiratory distress syndrome in patients with severe acute respiratory syndrome: a case control study. *BMC Infect Dis* 5, 26.
  21. **Chiu, RWK**, Chim, SSC, Tong, YK, Fung, KSC, Chan, PKS, Zhao, GP and Lo, YMD (2005). Tracing SARS-coronavirus variant with large genomic deletion. *Emerg Infect Dis* 11, 168-170.
  22. \*Chung, GTY, \***Chiu, RWK**, Chan, KCA, Lau, TK, Leung, TN and Lo, YMD (2005). Lack of dramatic enrichment of fetal DNA in maternal plasma by formaldehyde treatment. *Clin Chem* 51, 655-658. (Equal first author)

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23. Lo, YMD, **Chiu, RWK**, Chan, KCA and Chung, GTY (2004). Free fetal DNA in maternal circulation. *JAMA* 292, 2835.
  24. Lee, N, Chan, KCA, Hui, DSC, Ng, EKO, Wu, A, **Chiu, RWK**, Wong, VW, Chan, PK, Wong, KT, Wong, E, Cockram, CS, Tam, JS, Sung, JJS and Lo, YMD (2004). Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients. *J Clin Virol* 31, 304-309.
  25. **Chiu, RWK** and Lo, YMD (2004). The biology and diagnostic applications of fetal DNA and RNA in maternal plasma. *Curr Top Dev Biol* 61, 81-111.
  26. Farina, A, Chan, CWM, **Chiu, RWK**, Tsui, NBY, Carinci, P, Concu, M, Banzola, I, Rizzo, N and Lo, YMD (2004). Circulating corticotropin-releasing hormone mRNA in maternal plasma: relationship to gestational age and severity of preeclampsia. *Clin Chem* 50, 1851-4.
  27. **Chiu, RWK**, Tang, NLS, Hui, DSC, Chung, GTY, Chim, SSC, Chan, KCA, Sung, YM, Chan, LYS, Tong, YK, Lee, WS, Chan, PKS and Lo, YMD (2004). ACE2 Gene Polymorphisms Do Not Affect Outcome of Severe Acute Respiratory Syndrome. *Clin Chem* 50, 1683-1686.
  28. **Chiu, RWK** and Lo, YMD (2004). Recent Developments in Fetal DNA in Maternal Plasma. *Ann N Y Acad Sci* 1022, 100-104.
  29. Lo, YMD and **Chiu, RWK** (2004). The Biology and Diagnostic Applications of Plasma RNA. *Ann N Y Acad Sci* 1022, 135-139.
  30. Poon, TC, Chan, KCA, Ng, PC, **Chiu, RWK**, Ang, IL, Tong, YK, Ng, EKO, Cheng, FW, Li, AM, Hon, EK, Fok, TF and Lo, YMD (2004). Serial Analysis of Plasma Proteomic Signatures in Pediatric Patients with Severe Acute Respiratory Syndrome and Correlation with Viral Load. *Clin Chem* 50, 1452-1455.]
  31. \*Ding, C, \***Chiu, RWK**, Lau, TK, Leung, TN, Chan, LC, Chan, AY, Charoenkwan, P, Ng, IS, Law, HY, Ma, ES, Xu, X, Wanapirak, C, Sanguansermisri, T, Liao, C, Tan Jin Ai, MA, Chui, DHK, Cantor, CR and Lo, YMD (2004). MS analysis of single-nucleotide differences in circulating nucleic acids: Application to noninvasive prenatal diagnosis. *Proc Natl Acad Sci U S A*, 101, 10762-10767.  
(Equal first author)
  32. Tsui, NBY, Chim, SSC, **Chiu, RWK**, Lau, TK, Ng, EKO, Leung, TN, Tong, YK, Chan, KCA and Lo, YMD (2004). Systematic micro-array based identification of placental mRNA in maternal plasma: towards non-invasive prenatal gene expression profiling. *J Med Genet* 41, 461-467.
  33. Ng, EKO, El-Sheikhah, A, **Chiu, RWK**, Chan, KCA, Hogg, M, Bindra, R, Leung, TN, Lau, TK, Nicolaides, KH and Lo, YMD (2004). Evaluation of human

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chorionic gonadotropin beta-subunit mRNA concentrations in maternal serum in aneuploid pregnancies: a feasibility study. *Clin Chem* 50, 1055-1057.

34. **The Chinese SARS Molecular Epidemiology Consortium** (2004). Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. *Science* 303, 1666-1669. (Equal first author)
35. Chim, SSC, Tong, YK, Hung, ECW, **Chiu, RWK** and Lo, YMD (2004). Genomic sequencing of a SARS coronavirus isolate that predated the Metropole Hotel case cluster in Hong Kong. *Clin Chem* 50, 231-233.
36. Rainer, TH, Lam, NYL, Tsui, NBY, Ng, EKO, **Chiu, RWK**, Joynt, GM and Lo, YMD (2004). Effects of filtration on glyceraldehyde-3-phosphate dehydrogenase mRNA in the plasma of trauma patients and healthy individuals. *Clin Chem* 50, 206-208.
37. Lam, NYL, Rainer, TH, **Chiu, RWK**, Joynt, GM and Lo, YMD (2004). Plasma mitochondrial DNA concentrations after trauma. *Clin Chem* 50, 213-216.
38. Lam, NYL, Rainer, TH, **Chiu, RWK** and Lo, YMD (2004). EDTA is a better anticoagulant than heparin or citrate for delayed blood processing for plasma DNA analysis. *Clin Chem* 50, 256-257.
39. Hung, ECW, Chim, SSC, Chan, PK, Tong, YK, Ng, EKO, **Chiu, RWK**, Leung, CB, Sung, JJ, Tam, JS and Lo, YMD (2003). Detection of SARS Coronavirus RNA in the Cerebrospinal Fluid of a Patient with Severe Acute Respiratory Syndrome. *Clin Chem* 49, 2108-2109.
40. **Chiu, RWK**, Chim, SSC and Lo, YMD (2003). Molecular epidemiology of SARS-from Amoy Gardens to Taiwan. *N Engl J Med* 349, 1875-1876.
41. Ng, EKO, Ng, PC, Hon, KL, Cheng, WT, Hung, ECW, Chan, KCA, **Chiu, RWK**, Li, AM, Poon, LLM, Hui, DS, Tam, JS, Fok, TF and Lo, YMD (2003). Serial Analysis of the Plasma Concentration of SARS Coronavirus RNA in Pediatric Patients with Severe Acute Respiratory Syndrome. *Clin Chem* 49, 2085-2088.
42. Ng, EKO, Hui, DS, Chan, KCA, Hung, ECW, **Chiu, RWK**, Lee, N, Wu, A, Chim, SSC, Tong, YK, Sung, JJ, Tam, JS and Lo, YMD (2003). Quantitative Analysis and Prognostic Implication of SARS Coronavirus RNA in the Plasma and Serum of Patients with Severe Acute Respiratory Syndrome. *Clin Chem* 49, 1976-1980.
43. Chim, SSC, Tsui, SKW, Chan, KCA, Au, TC, Hung, ECW, Tong, YK, **Chiu, RWK**, Ng, EKO, Chan, PKS, Chu, CM, Sung, JJY, Tam, JS, Fung, KP, Waye, MMY, Lee, CY, Yuen, KY and Lo, YMD (2003). Genomic characterisation of the severe acute respiratory syndrome coronavirus of Amoy Gardens outbreak in Hong Kong. *Lancet* 362, 1807-1808.

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44. Tsui, SKW, Chim, SSC and Lo, YMD and the **Chinese Molecular SARS Research Group** (2003). Coronavirus genomic-sequence variations and the epidemiology of the severe acute respiratory syndrome. *N Engl J Med* 349, 187-188.
  45. Ng, EKO, Leung, TN, Tsui, NBY, Lau, TK, Panesar, NS, **Chiu, RWK** and Lo, YMD (2003). The concentration of circulating corticotropin-releasing hormone mRNA in maternal plasma is increased in preeclampsia. *Clin Chem* 49, 727-731.
  46. Ng, EKO, Tsui, NBY, Lau, TK, Leung, TN, **Chiu, RWK**, Panesar, NS, Lit, LCW, Chan, KW and Lo, YMD (2003). mRNA of placental origin is readily detectable in maternal plasma. *Proc Natl Acad Sci U S A* 100, 4748-4753.
  47. **Chiu, RWK**, Chan, LYS, Lam, NYL, Tsui, NBY, Ng, EKO, Rainer, TH and Lo, YMD (2003). Quantitative analysis of circulating mitochondrial DNA in plasma. *Clin Chem* 49, 719-726.
  48. **Chiu, RWK** and Lo, YMD (2003). Non-invasive prenatal diagnosis: on the horizon? *Pharmacogenomics* 4, 191-200.
  49. Chan, AKC, **Chiu, RWK** and Lo, YMD (2003). Cell-free nucleic acids in plasma, serum and urine: a new tool in molecular diagnosis. *Ann Clin Biochem* 40, 122-130.
  50. **Chiu, RWK**, Lau, TK, Leung, TN, Chow, KCK, Chui, DHK and Lo, YMD (2002). Prenatal exclusion of beta thalassaemia major by examination of maternal plasma. *Lancet* 360, 998-1000.
  51. Ng, EKO, Tsui, NBY, Lam, NY, **Chiu, RWK**, Yu, SC, Wong, SC, Lo, ES, Rainer, TH, Johnson, PJ and Lo, YMD (2002). Presence of filterable and nonfilterable mRNA in the plasma of cancer patients and healthy individuals. *Clin Chem* 48, 1212-1217.
  52. **Chiu, RWK**, Lau, TK, Cheung, PT, Gong, ZQ, Leung, TN and Lo, YMD (2002). Noninvasive prenatal exclusion of congenital adrenal hyperplasia by maternal plasma analysis: a feasibility study. *Clin Chem* 48, 778-780.
  53. **Chiu, RWK**, Ho, CS, Tong, SF, Ng, KF and Lam, CW (2002). Evaluation of a new handheld biosensor for point-of-care testing of whole blood beta-hydroxybutyrate concentration. *Hong Kong Med J* 8, 172-176.
  54. Lui, YYN, Chik, KW, **Chiu, RWK**, Ho, CY, Lam, CW and Lo, YMD (2002). Predominant hematopoietic origin of cell-free DNA in plasma and serum after sex-mismatched bone marrow transplantation. *Clin Chem* 48, 421-427.

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55. **Chiu, RWK** and Lo, YMD (2002). Application of fetal DNA in maternal plasma for noninvasive prenatal diagnosis. *Expert Rev Mol Diagn* 2, 32-40.
  56. **Chiu, RWK**, Poon, LLM, Lau, TK, Leung, TN, Wong, EMC and Lo, YMD (2001). Effects of blood-processing protocols on fetal and total DNA quantification in maternal plasma. *Clin Chem* 47, 1607-1613.
  57. Chan, MHM, Mak, TWL, **Chiu, RWK**, Chow, CC, Chan, IHS and Lam, CWK (2001). Simvastatin increases serum osteocalcin concentration in patients treated for hypercholesterolaemia. *J Clin Endocrinol Metab* 86, 4556-4559.
  58. **Chiu, RWK**, Murphy, MF, Fidler, C, Wainscoat, JS and Lo, YMD (2001). Technical optimization of RhD zygosity determination by real-time quantitative polymerase chain reaction: implication for fetal RhD status determination by maternal plasma. *Ann N Y Acad Sci* 945, 156-160.
  59. **Chiu, RWK**, Murphy, MF, Fidler, C, Zee, BC, Wainscoat, JS and Lo, YMD (2001). Determination of RhD zygosity: comparison of a double amplification refractory mutation system approach and a multiplex real-time quantitative PCR approach. *Clin Chem* 47, 667-672.
  60. **Chiu, RWK**, Tai, HL and Lam, CW (2000). Alcoholic ketoacidosis in two Chinese patients. *Chin Med J (Engl)* 113, 1051-1053.

***Refereed books and monographs***

1. Lo, YMD and **Chiu, RWK** (*in press*). Principals of molecular biology. Fundamentals of Molecular Diagnostics. DE Bruns, ER Ashwood and CA Burtis. Philadelphia. Elsevier Saunders.
2. Lo, YMD and **Chiu, RWK** (*in press*). Nucleic Acid Isolation. Fundamentals of Molecular Diagnostics. DE Bruns, ER Ashwood and CA Burtis. Philadelphia. Elsevier Saunders.
3. Lo, YMD, **Chiu, RWK**, Wittwer, CT and Kuskawa, N. (*in press*). Nucleic Acids. Tietz Fundamentals of Clinical Chemistry (6<sup>th</sup> Ed.). CA Burtis, ER Ashwood and DE Bruns. Philadelphia. Elsevier Saunders.
4. Lo, YMD, **Chiu, RWK** and Chan, KCA, Eds (2006). Clinical Applications of PCR. Humana Press: pp. 200.
5. **Chiu, RWK** and Lo, YMD (2006). Noninvasive prenatal diagnosis by analysis of fetal DNA in maternal plasma. Clinical Applications of PCR (2<sup>nd</sup> Ed.). YMD Lo, RWK Chiu and KCA Chan. Humana Press: 101-109.

6. Chim, SSC, **Chiu, RWK** and Lo, YMD (2006). Genomic Sequencing of the SARS Coronavirus. Clinical Applications of PCR (2<sup>nd</sup> Ed.). YMD Lo, RWK Chiu and KCA Chan. Humana Press: 177-194.
7. **Chiu, RWK** and Lo, YMD (2006). Mapping of the Global SARS Epidemic by Molecular Epidemiology. Challenges of Severe Acute Respiratory Syndrome. JCK Chan and VCW Taam Wong. Elsevier: 43-58.
8. **Chiu, RWK** and Lo, YMD (2005). Circulating Nucleic Acids – Diagnostic Potential. Encyclopedia of Medical Genomics and Proteomics. Marcel Dekker.
9. Lo, YMD and **Chiu, RWK** (2005). Principles of molecular biology and approaches to nucleic acid isolation. Tietz Textbook of Clinical Chemistry (4<sup>th</sup> Ed.). CA Burtis, ER Ashwood and DE Bruns. Philadelphia. Elsevier Saunders: 1393-1406.
10. **Chiu, RWK** and Lo, YMD (2002). Preanalytical issues for circulating DNA analysis: technical aspects, semantics and need for standardization. Molecular testing in laboratory medicine: selections from Clinical Chemistry 1998-2001. DE Bruns, YMD Lo and CT Wittwer. Washington, AACC Press: 309-310.
11. Lo, YMD, **Chiu, RWK** and Johnson, PJ, Eds. (2001). Circulating Nucleic Acids in Plasma or Serum 2. Annals of the New York Academy of Sciences. New York, New York Academy of Sciences.

#### **Conference abstracts**

1. Chow, KCK, **Chiu, RWK**, Tsui NBY, Ding, C, Lau, TK, Leung, TN, Lo, YMD (2006). Mass spectrometric detection of a SNP panel as internal positive controls for fetal DNA analysis in maternal plasma. 13th International Conference on Prenatal Diagnosis and Therapy, Kyoto, Japan.
2. Tsui, NBY, **Chiu, RWK**, Lui, WB, El-Sheikhah, A, Chan, ATC, Nicolaides, KH and Lo, YMD (2005). Development and Evaluation of an automated method for circulating fetal RNA extraction. *Clin Chem* 51, P75.
3. Tsui, NBY, **Chiu, RWK**, Chim, SSC, Tong, YK, Lau, TK, Leung, TN and Lo, YMD (2005). Placental RNA in maternal plasma: towards non-invasive fetal gene expression profiling. *Clin Chem* 51, S11.
4. Tong, YK, Lun, FMF, Chim, SSC, **Chiu, RWK**, Chan, LYS, Lau, TK, Leung, TN, Ding, C and Lo, YMD (2005). Hypomethylated maspin DNA sequences as a marker for preeclampsia. *Clin Chem* 51, P19a.
5. **Chiu, RWK**, Ding, C, Lau, TK, Leung, TN, Chan, LC, Chan, AYY, Charoenkwan, P, Ng, ISL, Xu, XM, Wanapirak, C, Sanguansermsri, T, Liao, C, Ma, ES, Chui, DHK, Cantor, CR and Lo, YMD (2003). Mass spectrometric



- analysis of fetal DNA in maternal plasma: Non-invasive prenatal diagnosis of beta-thalassemia. *Clin Chem* 49, S12.
6. **Chiu, RWK**, Chan, LYS, Lam, NYL, Tsui, NBY, Ng, EKO, Wong, BCK, Rainer, TH and Lo, YMD (2003). Circulating mitochondrial DNA analysis: quantitative analysis. *Clin Chem* 49, S19.
  7. **Chiu, RWK**, Tsui, NBY, Chim, SSC, Ng, EKO, Tong, YK, Lau, TK, Leung, TN and Lo, YMD (2003). Microarray-based identification of placenta-derived mRNA markers for detection in maternal plasma: towards non-invasive prediction of preeclampsia. *Am J Hum Genet* 73, 189.
  8. Ding, C, **Chiu, RWK**, Lau, TK, Leung, TN, Chan, LC, Chan, AYY, Charoenkwan, P, Ng, ISL, Xu, XM, Wanapirak, C, Sanguansermsri, T, Liao, C, Ma, ES, Chui, DHK, Cantor, CR and Lo, YMD (2003). Non-invasive prenatal diagnosis of beta-thalassemia by mass spectrometric analysis of fetal DNA in maternal plasma. *Am J Hum Genet* 73, 189.
  9. **Chiu, RWK**, Ding, C, Lau, TK, Leung, TN, Chan, LC, Chan, AYY, Charoenkwan, P, Ng, ISL, Xu, XM, Wanapirak, C, Sanguansermsri, T, Liao, C, Ma, ES, Chui, DHK, Cantor, CR and Lo, YMD (2003). Non-invasive prenatal diagnosis of  $\beta$ -thalassaemia by mass spectrometric analysis of fetal DNA in maternal plasma. 9th International conference on Thalassaemia and the Haemoglobinopathies & 11th International TIF conference for Parents and Thalassaemics, Palermo, Italy.
  10. **Chiu, RWK**, Lau, TK, Leung, TN, Chow, KCK, Chui, DHK and Lo, YMD (2002). Non-invasive prenatal exclusion of  $\beta$ -thalassaemia major through fetal DNA analysis in maternal plasma. The 4th HUGO Pacific Meeting and 5th Asia-Pacific Conference on Human Genetics, Pattaya, Thailand.
  11. **Chiu, RWK**, Chan, LYS, Tong, SF and Lo, YMD (2002). Effects of primer-specificity on the molecular analysis of the mitochondrial genome. *Clin Chem Lab Med* 40, S153.
  12. **Chiu, RWK**, Lau, TK, Gong, ZQ, Cheung, PT, Leung, TN and Lo, YMD (2001). Non-invasive prenatal diagnosis of congenital adrenal hyperplasia through the use of fetal DNA in maternal plasma. *Am J Hum Genet* 69, 666.
  13. **Chiu, RWK**, Ho, CS, Tong, SF, Ng, KF and Lam, CW (2001). Evaluation report of a point-of-care blood ketone sensor. Challenges and Opportunities in Pathology, Hong Kong.
  14. **Chiu, RWK**, Murphy, MF, Fidler, C, Wainscoat, JS and Lo, YMD (2001). Rapid determination of RhD zygosity by real-time quantitative polymerase chain

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reaction: implication for fetal RhD status determination by maternal plasma. *Clin Chem* 47, 369.

***Invited presentations***

1. "Applications of Fetal Nucleic Acids in Maternal Plasma for the Detection and Monitoring of Preeclampsia". Symposium in Preinatal Medicine 2006, organized by the Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, 24 September 2004.
2. "Detection of Fetal Point Mutations in Maternal Plasma". Second Asia Pacific Congress in Maternal Fetal Medicine, Guangzhou, China, organized by the Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, 22 September 2006.
3. "Fetal DNA in Maternal Plasma: from Research to Clinical Application". Symposium in Preinatal Medicine 2004, organized by the Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, 19 September 2004.
4. "Molecular Diagnostics for Acute Pathologies: New Applications of Circulating Nucleic Acids Analysis". Satellite Symposium on Neurochemical Monitoring, organized by Department of Surgery, The Chinese University of Hong Kong, 21 August 2004.
5. "Pre-analytical and Analytical Issues of Plasma Nucleic Acid Analysis". American Association of Clinical Chemistry Annual Meeting 2004, organized by American Association of Clinical Chemistry, Los Angeles, 26 July 2004.
6. "Circulating nucleic acids: Biology and diagnostics." Second Chinese Congress of Clinical Chemistry and Laboratory Medicine and the Sixth National Conference of Laboratory Medicine, Nanjing, China, Chinese Medical Association, 25 June 2004.
7. "Molecular Epidemiology of SARS." Hong Kong SARS Forum and Hospital Authority Convention 2004, Hospital Authority, Hong Kong, 9 May 2004.
8. "Caught in the act: the molecular evolution of the SARS-coronavirus." Users Group Meeting for Genetic analysis and Real-time PCR, organized by Applied Biosystems, Hong Kong, 2 April 2004.
9. "Diagnosis, monitoring, and prognostication of SARS using real time PCR: from research to routine application." Scientific Seminar on Real-time PCR Technology, organized by the Hong Kong Association of Medical Laboratories, 1 April 2004.

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10. "SARS: From molecular epidemiology to new diagnostic tests." Second China-Japan Symposium on Infectious Diseases, Hong Kong University of Science and Technology, 18 February 2004.
  11. "Interpretation of EQA." Quality Congress, Singapore Association of Clinical Biochemists, Singapore, 15 February 2004.
  12. "Will My Heart Go On: Reliable Troponins?" COC Pathology Commissioned Training Programme, COC Pathology, Hospital Authority, Hong Kong, 5 February 2004.
  13. "Fetal nucleic acids in maternal plasma: Towards non-invasive prenatal diagnosis." The 6th Chinese Laboratory Medicine Conference, Medical Technology Association, Hong Kong, 15 November 2003.
  14. "Interpretation of EQA." Workshop on External Quality Assessment, Hong Kong Society of Clinical Chemistry, and Division of Clinical Biochemistry, Queen Mary Hospital, 5 July 2003.
  15. "Non-invasive prenatal diagnosis of beta-thalassaemia." Symposium on Perinatal Medicine, Department of Obstetrics and Gynaecology, Prince of Wales Hospital, and CUHK, 7 September 2002.
  16. "Non-invasive prenatal diagnosis by fetal nucleic acids analysis in maternal plasma – from research to clinical application." Grand Round/Research Seminar at the Royal Children's Hospital Campus, Melbourne, Australia, 3 September 2003.
  17. "New advances in non-invasive prenatal diagnosis." Clinical Ligand Assay Society National Meeting: Frontiers in Laboratory Diagnostics, Houston, Texas, USA, 22 May 2002.

***Non-refereed publication***

1. **Chiu, RWK**, Chan, KCA, and Lo YMD (2004). Quality issues in SARS testing: experience from The Chinese University of Hong Kong. The Newsletter of the Asian and Pacific Federation of Clinical Biochemistry 2004 Issue, 34-35.
2. **Chiu, RWK**, Chan, AYW, Chan, MHM, Lam, CW, Mak, TWL, Shek, ACC, Tai, MHL, and Tam S (2004). Chemical pathology case conference – liver function tests. *HK Pract* 26, 430-435.
3. **Chiu, RWK** and Lo, YMD (2000). Fetal DNA in maternal plasma: Biological and Diagnostic implications. *HKJGOM* 1, 116-120.

## RESEARCH GRANTS:

### *External Competitive Research Grants*

	Title	Role	Funding Source HK\$, project period
1.	Biological and molecular characterization of placental-expressed mRNA in maternal plasma	Principal Investigator	Research Grants Council Competitive Earmarked Grant (CUHK4433/06M) HK \$654,500 01/10/2006 to 30/09/2007
2.	Investigation of the quantitative relationship between fetal nucleic acids in maternal plasma and fetal growth	Principal Investigator	Research Grants Council Competitive Earmarked Grant (CUHK4434/05M) HK \$854,018 01/01/2006 to 31/12/2007
3.	Quantitative aberrations in circulating RNA in maternal plasma: clinical and biological implications in preeclampsia	Principal Investigator	Research Grants Council Competitive Earmarked Grant (CUHK4277/04M) HK \$680,000 20/12/2004 to 19/12/2006
4.	Non-invasive prenatal diagnosis of $\beta$ -thalassaemia through maternal plasma analysis: a multi-centre collaborative study	Principal Investigator	Research Grants Council Competitive Earmarked Grant (CUHK4395/03M) HK \$886,200 15/12/2003 to 14/12/2006
5.	Centre for research into circulating fetal nucleic acids	Deputy Director	Major Area in Biomedical Sciences HK\$ 13,000,000 01/07/2006 to 30/06/2012
6.	Research into Circulating Fetal Nucleic Acids	Co-investigator	Li Ka Shing Institute of Health Sciences HK \$2,500,000 01/11/2005 to 31/10/2008
7.	A Centre for the study of fetal nucleic acids in maternal plasma	Co-investigator	Research Grants Council Central Allocation 2003-2004 (CUHK1/03C) HK \$4,400,000 + HK \$1,000,000 (CUHK supplementary funding) 01/03/2004 to 28/02/2007
8.	Development of genomic strategies for the non-invasive detection of Down syndrome	Deputy Project Coordinator	The Innovation and Technology Fund (ITS/195/01) HK \$7,653,385 01/04/2002 to 30/9/2007
9.	Application of functional genomics in human placenta and quantification of placental mRNA in maternal plasma of study of term and preterm parturition	Co-investigator	Research Grants Council Competitive Earmarked Grant (CUHK4484/06M) HK \$924,595 01/01/2007 to 31/12/2008

10	Methylation analysis of the RASSF1A gene in the placenta and in the plasma of pregnant women	Co-investigator	Research Grants Council Competitive Earmarked Grant (CUHK4437/05M) HK \$901,772 01/08/2005 to 31/07/2007
11	Development of maspin as an epigenetic fetal DNA marker in maternal plasma for all pregnancies	Co-investigator	Research Grants Council Competitive Earmarked Grant (CUHK4279/04M) HK \$811,200 06/08/2004 to 05/08/2006
12	Quantitative analysis of placental RNA in maternal plasma	Co-investigator	Research Grants Council Competitive Earmarked Grant (CUHK4474/03M) HK \$996,200 01/09/2003 to 31/08/2005
13	Quantitative analysis of plasma viral and host RNA in severe acute respiratory syndrome	Co-investigator	Research Grant Council Special Grant for SARS Research (CUHK4508/03M) HK \$415,800 01/07/2003 to 30/06/2004

#### ***CUHK Direct Grant Scheme***

	<b>Title</b>	<b>Role</b>	<b>Year</b>
1.	Origins of circulating mRNA in maternal plasma	Principal Investigator	2003
2.	Quantitative analysis of circulating mitochondrial DNA	Principal Investigator	2002
3.	Non-invasive prenatal screening of $\beta$ -thalassaemia by molecular analysis of maternal plasma	Principal Investigator	2000
4.	Investigation into circulating cell-free RNA in maternal plasma	Co-investigator	2001
5.	Development of a maternal plasma RNA marker for preeclampsia	Co-investigator	2002
6.	Development of maspin as an epigenetic fetal DNA marker in maternal plasma for all pregnancies	Co-investigator	2003
7.	Evaluation of human chorionic gonadotropin mRNA in maternal plasma as a potential marker for early diagnosis of ectopic pregnancy	Co-investigator	2003
8.	Identification of fetal-specific microRNAs in maternal plasma	Co-investigator	2005

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## OTHER RESEARCH CONTRIBUTIONS:

- Member of Research Committee, the Centre for Emerging Infectious Diseases
- Member of the CUHK Molecular SARS Research Group
- Member of the Chinese SARS Molecular Epidemiology Consortium
- Reviewer for *Clinical Chemistry, Prenatal Diagnosis, American Journal of Obstetrics and Gynecology, Biotechniques, Diabetic Medicine, Hong Kong Medical journal*
- Internal Reviewer for Competitive Earmarked Grant submissions, Medicine Panel, The Chinese University of Hong Kong

## SERVICES

1. Convenor of Chemical Pathology Quality Assurance Programme, Hong Kong College of Pathologists 2006-2007.
2. Member of the Specialty Board in Chemical Pathology, Hong Kong College of Pathologists 2006-2007.
3. Member of the Inspectors of Laboratories for Training in Chemical Pathology, Hong Kong College of Pathologists 2006-2010.
4. Teaching of a workshop titled, "Interpretation of commonly used blood results" in the Intern's workshop series organised for interns of the New Territories East Cluster of Hospitals.
5. Member of the Committee on Education and Curriculum Development of the International Federation of Clinical Chemistry and Laboratory Medicine 2005 - 2007
6. Immediate Past President 2006-2007 of the Hong Kong Society of Clinical Chemistry
7. President 2004-2005 of the Hong Kong Society of Clinical Chemistry
8. President-elect 2002-2003 of the Hong Kong Society of Clinical Chemistry
9. Member of Education Committee of the Hong Kong Society of Clinical Chemistry, 2002 - 2005
10. Member of Grants and Awards Committee of the Hong Kong Society of Clinical Chemistry, 2002 - 2005
11. Member of the Editorial Board for the Hong Kong Society of Clinical Chemistry Newsletter, 2000 - 2005
12. Convenor of Chemical Pathology Quality Assurance Programme, Hong Kong College of Pathologists 2004-2005
13. Scientific committee member for the 2<sup>nd</sup> Chinese Congress of Clinical Chemistry and Laboratory Medicine, 4-7 July 2004

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14. Organising committee member for the COC Pathology Commissioned Training 2003/2004, Hospital Authority
  15. Member of organising committee for the Hong Kong College of Pathologists and Hong Kong Society of Clinical Chemistry joint seminar: Herbal toxicology – A beginner's course for laboratory and clinical professionals (9<sup>th</sup> -10<sup>th</sup> March 2002)
  16. Member of local organising committee for the Second International Symposium on Circulating Nucleic Acids in Plasma and Serum held in conjunction with the 6<sup>th</sup> Annual Scientific Symposium of the Hong Kong Cancer Institute (20<sup>th</sup> – 21<sup>st</sup> February 2001).
  17. Social Committee member for Chinese Congress of Clinical Chemistry and Laboratory Medicine 2000

# Exhibit B



# **CURRICULUM VITAE**

**YUK-MING DENNIS LO**

***MA DM DPhil BM BCh MRCP (Lond) FRCP(Edin) FRCPath***

**NAME:** Yuk-Ming Dennis Lo

**DATE OF BIRTH:** 12th October, 1963

**MARITAL STATUS:** Married

**PROFESSIONAL ADDRESS:**

Department of Chemical Pathology,  
The Chinese University of Hong Kong,  
Prince of Wales Hospital,  
Shatin, New Territories,  
Hong Kong

*TELEPHONE NO.:* (+852) 2632 2963

*FAX NO.:* (+852) 2194 6171

*Email address:* loym@cuhk.edu.hk

**QUALIFICATIONS:**

Bachelor of Arts (Hons)	Cambridge	1986
Bachelor of Medicine & Bachelor of Surgery	Oxford	1989
Master of Arts	Cambridge	1990
Doctor of Philosophy	Oxford	1994
Member of the Royal College of Physicians	London	1995
Member of the Royal College of Pathologists	London	1999
Doctor of Medicine	Oxford	2001
Fellow of the Royal College of Physicians	Edinburgh	2004
Fellow of the Royal College of Pathologists	London	2005
Fellow of the Royal College of Physicians	London	2006

**SCHOLARSHIPS AND PRIZES**

- Emmanuel College Entrance Exhibition 1983-4
- College Senior Scholarship 1984-5
- G.G. Hooper Senior Scholarship 1985-6
- Colin MacKenzie Prize for outstanding performance  
in Tripos 1984-5  
1985-6
- Wing Tat Lee Elective Scholarship to the University  
of Hong Kong 1988-9
- L.J. Witts Prize in Haematology or Gastroenterology 1988-9

- Radcliffe Infirmary Prize in Pathology 1988-9
- Radcliffe Infirmary Prize in Medicine 1989-90
- Year Prize, Royal College of Pathologists 1989-90
- Carreras Senior Studentship in Natural Science, Hertford College, Oxford. 1990-1
- President's Prize (runner-up), Royal Society of Medicine, U.K. 1996
- Professors' Prize, Association of Professors of Academic Departments of Chemical Pathology 2000
- Awardee, Outstanding Young Person Selection (Hong Kong) 2000
- Leader of the Year Award, Technology Category 2000  
organised by SingTao Daily, Hong Kong iMail and CNBC
- Honoree, Outstanding Young Persons of the World Junior Chamber International 2001
- Avadesh Saran Memorial Oration Award 2002  
9<sup>th</sup> Asian Pacific Congress of Clinical Biochemistry
- National Natural Science Award, People's Republic of China 2005

#### **RESEARCH AWARDS**

- Wellcome Vacation Scholarship 1986
- Foulkes' Foundation Studentship 1988-9
- Royal College of Pathologists Bursary for Elective Studies in Pathology 1988-9
- Foulkes' Foundation Fellowship 1990-3
- Katherine Bishop Harman Award 1990-1  
British Medical Association
- Wellcome Medical Graduate Fellowship 1990-3
- Junior Research Fellowship in Medicine, Hertford College, Oxford 1991-4
- Croucher Senior Medical Research Fellowship 2005-6

#### **PROFESSIONAL TRAINING:**

I am a consultant-level staff running a busy chemical pathology service at a general 1360-bed hospital, the Prince of Wales Hospital in Hong Kong. Our laboratory is the first one in Hong Kong to be accredited under the National Association of Testing Authorities, Australia. We provide a full-range of laboratory diagnostic services, ranging from serum electrolytes to

toxicology to metabolic screening to molecular testing. Since 2003, we have also run a new serum RNA test for the SARS-coronavirus, developed locally by my group. I am fully participating in the on-call chemical pathology rota. I am also responsible for supervising the twice weekly duty biochemists' meeting during which clinical and management issues will be discussed.

In my previous appointment at the John Radcliffe Hospital, Oxford, I was one of the 3 Consultant Chemical Pathologists serving a 700-bed general hospital. I fully participated in the on-call rota and provided specialist consultation to clinical colleagues. I am a Fellow of the Royal College of Pathologists and a registrant on the Specialist Register in Chemical Pathology in the U.K.

During my postgraduate clinical training at Oxford, I worked as a Senior House Officer in General Medicine, Cardiology, Haematology, Infectious Diseases and Neurology. This has given me valuable clinical experience and allowed me to qualify for Membership of the Royal College of Physicians (London). I was elected to a Fellowship of the Royal College of Physicians (Edinburgh) in 2004.

I have listed my professional training with dates below:

House Physician, (under Prof. Michael Langman) Medical Professorial Unit and Department of Cardiology, Queen Elizabeth Hospital, Birmingham B15 2TH, U.K.	1989-90
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House Surgeon, (under Prof. Sir Peter Morris) Nuffield Department of Surgery, John Radcliffe Hospital, Oxford OX3 9DU, U.K.	1990-90
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Senior House Officer training (under Prof. John Bell) Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford OX3 9DU, U.K.	1994-5
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Honorary Registrar in Chemical Pathology, Radcliffe Hospital NHS Trust, John Radcliffe Hospital,	1995-6
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Oxford,  
U.K.

Honorary Consultant Chemical Pathologist,  
Radcliffe Hospital NHS Trust,  
John Radcliffe Hospital,  
Oxford,  
U.K.

1996-97

Honorary Consultant Chemical Pathologist,  
Prince of Wales Hospital,  
Shatin, New Territories,  
Hong Kong

1997-present

## **PROFESSIONAL APPOINTMENTS**

Li Ka Shing Professor of Medicine  
Faculty of Medicine  
The Chinese University of Hong Kong

1 September 2005-present

Director  
Li Ka Shing Institute of Health Sciences  
Faculty of Medicine  
The Chinese University of Hong Kong

1 September 2005-present

Professor of Chemical Pathology  
Faculty of Medicine,  
The Chinese University of Hong Kong

1 October 2003 - present

Associate Dean (Research),  
Faculty of Medicine,  
The Chinese University of Hong Kong

1 August 2002 - present

Reader,  
Department of Chemical Pathology,  
The Chinese University of Hong Kong

1 October 2000 – 30 September 2003

Senior Lecturer,  
Department of Chemical Pathology  
The Chinese University of Hong Kong

27 January 1997 – 1 October 2000

University Lecturer in Clinical Biochemistry  
University of Oxford,  
Nuffield Department of Clinical Biochemistry,  
U.K.

1994-97

Fellow, 1994-97  
Green College,  
Oxford,  
U.K.

Wellcome Clinician Scientist Fellow, 1993-94  
University of Oxford,  
Nuffield Department of Clinical Medicine,  
U.K.

Wellcome Medical Graduate Fellow, 1990-93  
University of Oxford,  
Nuffield Department of Pathology & Bacteriology,  
U.K.

#### **TEACHING AWARD**

- Awardee, Teacher of the Year (Med 3) 2001

#### **PROFESSIONAL SOCIETY MEMBERSHIPS:**

- |                                                     |               |
|-----------------------------------------------------|---------------|
| • American Association of Clinical Chemistry        | 1997- present |
| • American Society of Human Genetics                | 1998-present  |
| • Pathological Society of Great Britain and Ireland | 1990-present  |
| • Hong Kong Society of Clinical Chemistry           | 1997-present  |

#### **CONTRIBUTION TO DEPARTMENT/HOSPITAL/COMMUNITY:**

##### ***SERVICE TO ACADEMIA***

- Selection Committee Member, Esther Yewpick Lee Millennium Scholarships
- Convenor, Medicine Panel
- Member, Research Committee
- Member, Clinical Research Ethics Committee
- Member of Departmental Executive Committee
- Secretary, Departmental Board
- Coordinator, Departmental Molecular Biology Unit

- Member of Departmental Graduate Panel

### ***SERVICE TO PROFESSIONAL COMMUNITY***

- Honorary Professor, Nanjing Medical University, China
- Editorial Board Member, *Clinical Chemistry*, the official journal of the American Association for Clinical Chemistry
- Editorial Board Member, *Disease Markers*
- Asian-Pacific Federation of Clinical Biochemistry Travelling Lecturer 2001-2002
- PathCentre Visiting Lecturer 2002, Perth, Australia
- President, Hong Kong Society of Clinical Chemistry (2001-2003)
- Member, Biotechnology Projects Vetting Committee, Innovation and Technology Fund, Government of the Hong Kong SAR
- Council Member, Hong Kong Research Grants Council
- Panel Member, Biology & Medicine Panel, Hong Kong Research Grants Council
- Committee Member, Hong Kong Academy of Medicine Examinations Subcommittee
- Board Member, Hong Kong Science and Technology Parks Limited (2003-2005)
- Co-chairman, Organising Committee, 2<sup>nd</sup> International Symposium on Circulating Nucleic Acids in Plasma/Serum (19 to 21 February 2001)
- Adjudicator, Immigration Tribunal, Government of the Hong Kong SAR
- Executive Committee Member, Outstanding Young Persons' Association (2001-2002)
- Reviewer for *New England Journal of Medicine*, *Lancet*, *Proceedings of the National Academy of Sciences (USA)*, *Clinical Chemistry*, *Cancer Research*, *American Journal of Human Genetics*, *American Journal of Obstetrics & Gynecology*, *Clinical Cancer Research*, *Human Genetics*, *Molecular Human Reproduction*, *Prenatal Diagnosis*

## ***Publications***

1. **Lo YMD**, Mehal WZ, Fleming KA. False-positive results and the polymerase chain reaction. *Lancet* 1988; ii: 679.
2. **Lo YMD**, Mehal WZ, Fleming KA. Rapid production of vector-free biotinylated probes using the polymerase chain reaction. *Nucleic Acids Research* 1988; 16: 8719.
3. **Lo YMD**, Mehal WZ, Fleming KA. In vitro amplification of hepatitis B virus sequences from liver tumour DNA and from paraffin wax embedded tissues using the polymerase chain reaction. *Journal of Clinical Pathology* 1989; 42: 840-846.
4. **Lo YMD**, Patel P, Wainscoat JS, Sampietro M, Gillmer MDG, Fleming KA. Prenatal sex determination by DNA amplification from maternal peripheral blood. *Lancet* 1989; ii: 1363-1365.
5. **Lo YMD**, Patel P, Sampietro M, Gillmer MDG, Fleming KA, Wainscoat JS. Detection of a single-copy fetal DNA sequence from maternal blood. *Lancet* 1990; 335: 1463-1464.
6. **Lo YMD**, Lo E-SF, Patel P, Tse CH, Fleming KA. Heteroduplex formation as a means to exclude contamination in virus detection using PCR. *Nucleic Acids Research* 1991; 19: 6653.
7. **Lo YMD**, Mehal WZ, Wordsworth BP, Chapman RW, Fleming KA, Bell JI, Wainscoat JS. HLA typing by double ARMS. *Lancet* 1991 338: 65-66.
8. **Lo YMD**, Patel P, Newton CR, Markham AF, Fleming KA, Wainscoat JS. Direct haplotype determination by double ARMS: specificity, sensitivity and genetic applications. *Nucleic Acids Research* 1991; 19: 3561-3567.
9. Patel P, **Lo YMD**, Bell GI, Turner RC, Wainscoat JS. Dinucleotide repeat polymorphism at the human GLUT2 locus. *Nucleic Acids Research* 1991; 19: 4017.
10. \*Stoffel M, \*Patel P, **\*Lo YMD**, Hattersley AT, Lucassen AM, Bell JI, Bell GI, Turner RC, Wainscoat JS. Characterisation of a missense glucokinase mutation in maturity-onset diabetes of the young (MODY) and mutation screening in late-onset diabetes. *Nature Genetics* 1992; 2: 153-156. (\*equal first authors)
11. Hattersley AT, **Lo YMD**, Reid SJ, Eglin RP, Wainscoat JS, Clark A. Failure to detect cytomegalovirus DNA in pancreas in type 2 diabetes. *Lancet* 1992; 339: 459-460.



12. Lo ES-F, **Lo YMD**, Tse CH, Fleming KA. Detection of a hepatitis B pre-core mutant by allele specific polymerase chain reaction. *Journal of Clinical Pathology* 1992; 45: 689-692.
13. **Lo YMD**, Patel P, Mehal WZ, Fleming KA, Bell JI, Wainscoat JS. Analysis of complex genetic systems by ARMS-SSCP: application to HLA genotyping. *Nucleic Acids Research* 1992; 20: 1005-1009.
14. Patel P, **Lo YMD**, Bell JI, Wainscoat JS. Detection of susceptibility alleles to insulin-dependent diabetes mellitus at the DQB1 locus by artificial PCR-RFLP. *Immunogenetics* 1992; 36: 264-265.
15. Patel P, **Lo YMD**, Hattersley AT, Bell GI, Tybjaerg-Hansen A, Nerup J, Turner RC, Wainscoat JS. Linkage analysis of maturity-onset diabetes of the young with microsatellite polymorphisms: no linkage to ADA or GLUT2 genes in two families. *Diabetes* 1992; 41: 962-967.
16. Yap EP-H, **Lo YMD**, Cooper K, Fleming KA, McGee JO'D. False positive viral diagnosis by PCR: exclusion by single stranded conformation polymorphism (SSCP). *Lancet* 1992; 340: 736.
17. Gidh-Jain M, Takeda J, Wu LZ, Lange AJ, Vionnet N, Stoffel M, Velho G, Sun F, Cohen D, Froguel Ph, Patel P, **Lo YMD**, Hattersley AT, Luthman H, Wedell A, St Charles R, Harrison RW, Weber IT, Bell GI, Pilkis SJ. Glucokinase mutations associated with non-insulin-dependent (Type 2) diabetes mellitus have decreased enzymatic activity: Implications for structure/function relationships. *Proceedings of the National Academy of Sciences of the United States of America* 1993; 90: 1932-1936.
18. **Lo YMD**, Howell PJ, Selinger M, MacKenzie IZ, Chamberlain P, Gillmer MDG, Littlewood TJ, Fleming KA, Wainscoat JS. Prenatal determination of fetal RhD status by analysis of peripheral blood of rhesus negative mothers. *Lancet* 1993; 341: 1147-1148.
19. **Lo YMD**, Lo ES-F, Mehal WZ, Sampietro M, Fiorelli G, Ronchi G, Tse CH, Fleming KA. Geographical variation in prevalence of hepatitis B virus DNA in HBsAg negative patients. *Journal of Clinical Pathology* 1993; 46: 304-308
20. **Lo YMD**, Patel P, Baigent CN, Gillmer MDG, Chamberlain P, Travi M, Sampietro M, Wainscoat JS, Fleming KA. Prenatal sex determination from maternal peripheral blood using the polymerase chain reaction. *Human Genetics* 1993; 90: 483-488.

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## RECENT INVITED LECTURES

- "Plasma DNA as a new tool for molecular diagnosis", 4 December 1998, Plenary speaker for the Second Hong Kong Conference on Clinical Chemistry, Hong Kong
- "Plasma DNA as a new tool for molecular diagnosis", 8 March 1999, Invited speaker to the Shanghai Second Medical University, Shanghai

- "A New DNA Blood Test. International Telemedicine Seminars: Nasopharyngeal Cancer: the "Cantonese Tumor"; 24 June 1999, The Chinese University of Hong Kong (in collaboration with the University of Southern California)
- "Biological and diagnostic implications of circulating fetal DNA in maternal blood", 14 August 1999, Invited speaker at the 8th International Symposium of Society of Chinese Bioscientists in America (SCBA), Hong Kong
- "Fetal DNA in maternal plasma", 20 August 1999, Invited speaker at the First International Symposium on Circulating Nucleic Acids in Plasma/Serum, Annecy, France.
- "Two way traffic between mother and fetus", 8 October 1999, Invited speaker at the First International Symposium on Microchimerism in Human Diseases, Paris, France
- "Cell-free fetal DNA in maternal plasma: diagnostic and biological implications", 16 October 1999, Invited speaker at the 2nd Hong Kong Medical Genetics Conference, Hong Kong
- "Human plasma DNA: biological basis and clinical applications", 30 October 1999, Invited lecturer for a State-of-the-Art Lecture at the Joint Scientific Meeting between the Hong Kong College of Physicians and the Hong Kong College of Paediatricians, Hong Kong
- "Plasma DNA chimerism in health and disease", 20 November 1999, TB Teoh Foundation Lecture at the 8th Annual General Meeting, The Hong Kong College of Pathologists
- "Fetal DNA in maternal plasma", 20 June 2000, Invited speaker at the 10th International Conference on Prenatal Diagnosis and Therapy, Barcelona, Spain
- "Quantitative analysis of tumor-derived DNA in plasma and serum: biological and clinical implications", 25 March 2001, Invited speaker at the 92<sup>nd</sup> Annual Meeting of the American Association for Cancer Research, New Orleans, U.S.A.
- "Studies on bi-directional DNA trafficking", 12 May 2001, Invited Speaker at the 12<sup>th</sup> Fetal Cell Workshop. Prague, Czech Republic.
- "Fetal DNA in maternal plasma", 17 May 2001, Invited Symposium Speaker at the 11<sup>th</sup> International Congress of Human Genetics, Vienna, Austria.
- "Fetal DNA in maternal plasma: application to non-invasive blood group genotyping of the fetus", 18 July 2001, State-of-the-Art Lecturer at the VII European Congress of the International Society of Blood Transfusion, Paris, France.

- “Fetal DNA in maternal plasma” and “Plasma DNA as a new class of tumor marker”, 3 October 2001, Plenary and Symposium Speaker, respectively, at the 1<sup>st</sup> Asia Association of Medical Laboratory Scientists Congress, Kuala Lumpur, Malaysia.
- “Plasma DNA: biological and diagnostic implications”, 9 to 12 October 2001, Plenary Speaker at the 39<sup>th</sup> Meeting of the Australasian Association of Clinical Biochemists, Auckland, New Zealand.
- “Plasma DNA: a revolution in molecular diagnosis”, 30 January 2002, Keynote Speaker at the BioIT Expo 2002, Hong Kong
- “Plasma DNA as a new tool for molecular diagnosis”, 9 to 14 March 2002, Plenary Speaker at the 9<sup>th</sup> Asian Pacific Congress of Clinical Biochemistry, New Delhi, India.
- “Plasma-based DNA markers for the diagnosis of malignancy or cancer”, 6 April 2002, Plenary Speaker at the Scientific Meeting of the Indonesian Association of Clinical Chemistry, Jakarta, Indonesia.
- “Advances in Cancer Diagnosis”, 5 May 2002, Invited speaker at the Advances in Medicine 2002 conference, Hong Kong.
- Clinical applications of fetal DNA and RNA in maternal plasma”, 5 June 2002, Plenary Speaker at the 11<sup>th</sup> International Conference of Prenatal Diagnosis and Therapy, Buenos Aires, Argentina.
- “The biology and diagnostic applications of fetal DNA in maternal plasma”, 11 to 16 August 2002, Invited Speaker at the Gordon Research Conference on Molecular Cytogenetics, Bristol, Rhode Island, U.S.A.
- “Plasma Epstein-Barr virus DNA as a tool for post-treatment monitoring of EBV-associated malignancies”, 2 July 2002, Invited Symposium Speaker at the British Cancer Research Meeting 2002, Glasgow, U.K.
- “Non-invasive prenatal diagnosis: past, present and future”, 7 September 2002, Plenary Speaker at the Symposium on Perinatal Medicine, Hong Kong.
- “Plasma DNA as a new tool for molecular diagnosis”, 14 September 2002, Plenary Speaker at the National Youth Congress in Laboratory Medicine, Chengdu, China.
- “Fetal DNA in maternal plasma: towards non-invasive prenatal diagnosis”, 28 October 2002, Symposium Speaker at the 4<sup>th</sup> Human Genome Organization Pacific Meeting, Pattaya, Thailand.

- Roche Diagnostic Lecture, September 2003, International Society of Oncodevelopmental Biology and Medicine, Edinburgh, U.K.
- Plenary speaker, 3<sup>rd</sup> International Symposium on Circulating Nucleic Acids in Plasma and Serum (CNAPS-3), Santa Monica, CA, USA, October 2003.
- Workshop speaker, European Society of Human Genetics conference, Prague, May 2005.
- Plenary speaker, XIX International Congress on Clinical Chemistry, Orlando, USA, July 2005.
- Invited speaker, 4<sup>th</sup> International Symposium on Circulating Nucleic Acids in Plasma and Serum (CNAPS-4), London, September 2005.

# Exhibit C

